IN THE UNITED STATES PATENT AN D TRADEMARK OFFICE

Applicant: Robyn WARD *et al.*

Title: **ASSESSMENT OF DISEASE RISK BY QUANTITATIVE DETERMINATION OF EPIMUTATION IN NORMAL TISSUES**

Appl. No.: 10/576,575

International Filing Date: April 20, 2006

Examiner: Unassigned

Art Unit: 1634

Confirmation Number: 4121

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

On an accompanying Form PTO/SB/08 is a listing of documents that are known to applicants and that are submitted presently in cognizance of their duty pursuant to 37 CFR §1.56. Nevertheless, this submission, which is not a statutory bar, is not intended as an admission that any listed document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in Rule 56(b).

Applicants waive no right to take any action that would be appropriate to antedate or otherwise remove as a competent reference any document that is determined to be a *prima facie* art reference against the claims of this application.

TIMING OF THE DISCLOSURE

In keeping with 37 CFR §1.97(b), the listed documents are submitted before the mailing of a first Office Action on the merits.

REMARKS

Applicants note that the listed documents, an addendum and a letter to editor, are both authored by Hitchins and Ward and concern an article, by the present inventors, published in *Nature Genetics*. That article by Suter et al., *Nat. Genet.* 36: 497-501 (2004), in turn relates to information contained in the instant application. The addendum and letter advocate that new data call into question the notion of transgenerational epigenetic inheritance, which Suter *et al.* had discussed.

The assertions made by Hitchins and Ward on this point bear no relevance to the pending claims. That is, their contentions concern epimutation in sperm, while the claimed invention concerns assessing the risk of disease by determining the frequency of somatic epimutation.

The Hitchins/Ward assertions also are flawed factually. Their premise, that "SNRPN...is unmethylated in spermatozoa," is based on an assay (cited Reference A19) that is far less sensitive than their own PCR assay. Furthermore, they demonstrate SNRPN methylation in normal control spermatozoa (Figure 1 of Reference A20), in proportions equivalent to the proportion that they observe in TT. This result indicates that rare, methylated SNRPN alleles are not a valid indicator of somatic cell contamination.

In contrast, Suter *et al.* (2004) confirmed the purity of TT's spermatozoa with direct and extraordinarily sensitive measures of cellular composition (FACS, microscopy). Those data suggested a slightly imperfect resetting of SNRPN imprinting and confirmed a previous finding of the MLH1 epimutation in TT's spermatozoa.

Thus, the listed documents are deemed to be flawed scientifically and irrelevant to patentability of the pending claims. Nevertheless, applicants request that the examiner consider the listed documents, make each of record in the application, and return an initialed copy of Form PTO/SB/08, in accordance with MPEP §609.

The Commissioner also is authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this paper, then the Commissioner is authorized to charge the unpaid amount to the same deposit account.

Respectfully submitted,

Date 29 November 2007

By Reg No. 48,571

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

For Stephen A. Bent
Attorney for Applicant
Registration No. 29,768